Dual Prevention Pill

Market Preparation and Introduction Strategy

AUGUST 2021

AVAC 25 Years and Counting

CLINTON HEALTH ACCESS INITIATIVE

HIV Prevention Market Manager
Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact
AVAC 25 Years and Counting
Supported by the Bill & Melinda Gates Foundation

Mann Global Health

CIFF CHILDREN'S INVESTMENT FUND FOUNDATION

Table of Contents

I. Introduction

To accelerate the introduction of and access to the Dual Prevention Pill (DPP), a daily oral pill for HIV and pregnancy prevention, AVAC, Clinton Health Access Initiative (CHAI) and Mann Global Health, with support from the Children's Investment Fund Foundation (CIFF), have developed a *Market Preparation and Introduction Strategy for the DPP*. These organizations are part of a larger coalition — known as the DPP Consortium — working to bring the DPP to market.[1]

This strategy is intended for donors, governments, implementing partners and civil society to inform priorities and planning for DPP rollout. To this end, the strategy describes activities required to build a cohesive body of evidence and recommends an approach to DPP introduction to focus efforts. Activities are not intended to confer funding from any one donor. Where possible, activities will be embedded into existing programs to consolidate and leverage resources.

To develop the strategy, AVAC, CHAI and Mann Global Health:

Scoped and analyzed existing knowledge and evidence gaps along the research-to-rollout framework.

Sequenced, thematically organized and described activities required to build a cohesive body of evidence to support scaling of the DPP.

Validated assumptions and approach with key stakeholders, including policy makers, donors, implementing partners and civil society.

Will iterate as new evidence and information become available to respond to a dynamic prevention landscape and as activities outlined in the strategy are completed.

About the DPP Consortium

The DPP Consortium is coalition of organizations, including AVAC, CHAI, Mann Global Health, Viatris and the Population Council, that are implementing market preparation and introduction activities for the DPP. These efforts are supported by CIFF, the Bill & Melinda Gates Foundation (BMGF), the U.S. Agency for International Development (USAID) and WCG Cares.

II. The Product and the User

The DPP would be the first product since male and female condoms to provide women[i] with a single option for HIV prevention and family planning (FP). Therefore, it offers a critical opportunity to assess whether uptake and effective use of biomedical HIV prevention increases with a multi-purpose prevention technology (MPT).

1. The product

a. Composition and packaging of the DPP

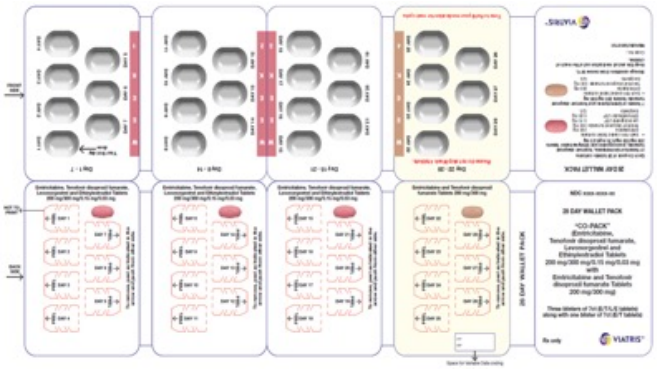
The DPP is a daily oral pill for HIV and pregnancy prevention with a 28-day regimen:

- **Days 1-21:** Tenofovir/emtricitabine (TDF/FTC, or oral PrEP) + levonorgestrel and ethinyl estradiol (LNG/EE, or combined oral contraception (COC))[ii]
- **Days 22-28:** TDF/FTC only (corresponding to COC placebo days)

The DPP will initially be developed and manufactured by Viatris (formerly Mylan), a generic manufacturer of oral contraceptives (OCs) and antiretrovirals. The DPP is being developed as a co-formulated bi-layer tablet, with differentiated colors for the first 21 vs. last 7 days. Pills will be dark pink and light peach, respectively, which were preferred among seven color options by end users in human-centered design (HCD) research conducted in South Africa and Zimbabwe.[2]

Figure 1: Proposed DPP tablet colors

Figure 2: Illustrative mock-up of DPP packaging by Viatris



The co-formulated DPP developed by Viatris will be packaged in a cold-form blister in an accordion-style wallet pack, with instructions for use printed on the pack to ensure correct use and mitigate user error. Each week will include a perforation, allowing end users to tear off sheets weekly. Branding will have a women's lifestyle feel and be developed in consultation with end users and civil society advocates.

Current regulatory timelines suggest the DPP developed by Viatris could receive **US Food & Drug Administration (FDA) approval in 2024**. The DPP Consortium will assess opportunities to bring other suppliers to market to encourage competition so as to increase affordability and supply security.

i The term "women" is used throughout the strategy to describe the initial focus population for the DPP. Additional research or consultation is needed to determine if the DPP is safe and effective for transgender men and non-binary individuals to use.

ii Throughout the strategy, the term "oral PrEP" refers specifically to TDF/FTC (brand name Truvada) and daily oral pill-taking, while the term "PrEP" refers to all delivery methods for pre-exposure prophylaxis, inclusive of CAB-LA and the Dapivirine Vaginal Ring. The term "COC" refers to the hormonal oral contraceptive formulation that the DPP contains (LNG/EE), whereas "OC" refers to oral contraception more generally, e.g., to describe preferences or behaviors around pill-taking that may be generalizable across OC products.

b. How does the DPP respond to end-user preferences?

End-user research studies have shown evidence of a demand for MPTs that prevent HIV and pregnancy. Discreet choice experiments suggest a higher demand for MPTs among women interested in HIV prevention compared to single-indication products.[3] For instance, the Tablets, Ring, Injections as Options (TRIO) study, conducted with women ages 18-30 in Kenya and South Africa, found participants "overwhelmingly" preferred a combined product for HIV and pregnancy prevention compared to two separate products, and that most were willing to forego their preferred single-indication product (injection) for a less-preferred product form that offered dual protection.[4] In the CUPID study, 91% of heterosexual couples in Uganda and Zimbabwe preferred MPTs over separate HIV prevention and FP products, and male partners were found to strongly contribute to women's decisions on product preferences.[5] This literature establishes a case for the development of MPTs to respond to end users' stated preferences.

c. What does the DPP offer?

As a woman-centered and controlled option that prevents HIV and pregnancy, the DPP has the potential to reach more women with oral PrEP, improve effective use and, by extension, contribute to decreased HIV incidence and unintended pregnancies. An initial Value for Money analysis was conducted to quantify both the public health and economic costs and benefits of the product. The DPP is uniquely positioned to bridge HIV and FP siloes in funding, research, health systems and service delivery. Lessons from the process of introducing and scaling the DPP, and related health systems adaptations – most notably, HIV/SRH service integration – would benefit and may accelerate rollout of future long-acting MPTs, such as vaginal rings, injectables and implants.[6]

While the DPP is likely to be introduced in parallel with the dapivirine vaginal ring (the ring) and long-acting cabotegravir (CAB-LA), these latter two products do not provide contraceptive benefits – a concern that is top-of-mind for women.[7] The DPP is not intended to compete with or reverse trends in use of long-acting reversible contraceptives (LARCs), and instead will provide an alternative option for women who prefer the flexibility of short-acting contraceptives that are immediately reversible and user-controlled, and for whom daily pill-taking is not a barrier.

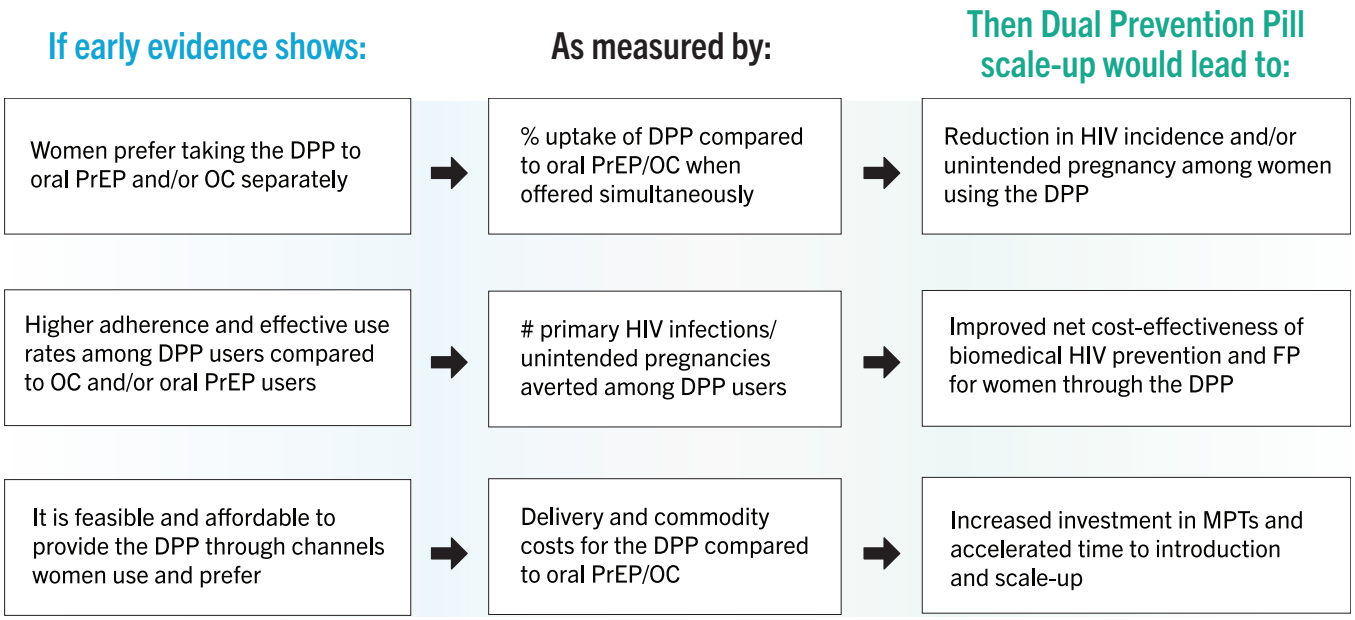
Figure 3: Potential benefits and risks associated with the DPP, by audience

Stakeholder	Potential Benefits	Potential Risks and Mitigation Plans
End Users	**Combined use can lead to better health outcomes.** A single co-formulated pill affords convenience – with protection from unintended pregnancy motivating women to adhere and continue use, including during periods of lower perceived HIV risk.[8] **A woman-controlled MPT.** The DPP affords women greater agency to mediate use. Women can mask the DPP as contraception to avoid the negative perceptions associated with oral PrEP. The DPP can potentially be marketed as "contraception plus." **Brings PrEP closer to women and builds on a shift toward self-care.** While FP is available in a variety of settings, PrEP is primarily offered in HIV clinics. As "contraception plus," the DPP may provide an impetus to re-evaluate antiretroviral (ARV) training requirements to better support integrated delivery with FP and other sexual health services, including via more decentralized delivery channels. It may also simplify access, requiring one clinic visit instead of multiple visits for separate products.	**Insufficient uptake and effective use, given that both OC and oral PrEP have high rates of early discontinuation and oral PrEP awareness is low in many settings.** Extensive end-user research will be conducted prior to introduction and draw on lessons learned from OC and oral PrEP to understand how to best engage users and support women to initiate the DPP and sustain use. Shifts to simplified, self-care approaches to oral PrEP delivery are being piloted and scaled. These better align with OC delivery and could bolster uptake and adherence to the DPP. Implementation research in real-world settings will test and evaluate delivery approaches, including how HIV testing factors into service provision and how rapid HIV and pregnancy testing can be done in parallel.

Figure 3: Potential benefits and risks associated with the DPP, by audience

Stakeholder	Potential Benefits	Potential Risks and Mitigation Plans
Providers	**Streamlines delivery of HIV and FP.** Long term, the DPP has the potential to reduce the burden on providers by delivering integrated services within a product, but this will rely on a move toward rational distribution of providers, HIV/SRH service integration and capacitation of FP providers, pharmacists and other cadres to offer HIV prevention and, in the interim, information on the DPP and where to access it.	**Providers may be reluctant to offer the DPP** because it feels like an added burden or due to stigmatizing beliefs such as the perception it could encourage younger women to have sex and/or multiple partners. A working group of HIV and SRH clinical and programmatic experts will develop recommendations for provider counseling messages, to be tested in DPP acceptability studies. Robust civil society engagement will build literacy on the DPP in communities in advance of rollout, providing additional touchpoints for education outside of clinics.
	Enables providers to respond to women's needs. By expanding options and addressing multiple health needs, the DPP may increase women's satisfaction – a motivating factor for providers.	
Policy makers/ government	**Lays the groundwork for MPT introduction and evidence generation.** The DPP can bypass a large clinical trial because it combines two approved products, offering a near-term opportunity to test hypotheses on the potential improved coverage and hence population-level impact of an MPT. Future MPTs are likely to build on the regulatory, delivery and financing lessons generated from DPP introduction and scale-up.	**Difficulty bridging historically siloed HIV and FP programs to deliver an MPT, including separate budgets and supply chains.** Strengthening HIV/FP linkages and platforms for the DPP ahead of approval will ready health systems for other MPTs and potentially also benefit the introduction of the ring and CAB-LA. Adding a product with HIV prevention to both the current HIV prevention and contraceptive method mix will require greater, more intentional coordination. Growing commitment, momentum and mechanisms for integrating HIV prevention and SRH services can improve coordination across departments to facilitate DPP introduction.
	Competitive with oral PrEP/COC separately. If DPP use increases over time, the DPP may be lower cost than oral PrEP and COC purchased individually depending on manufacturer pricing.	**With a single manufacturer for the DPP initially, supply security and affordability may be an initial concern of governments, and could deter procurement in favor of separate oral PrEP/COC.** Market shaping should be explored to expand the number of manufacturers in line with demand and to improve the value for money in commodity procurement. It will be critical to ensure these efforts do not deter procurement of oral PrEP and sensitization may be required to ensure oral PrEP remains a priority for those for whom the DPP may not be appropriate, including women on LARCs.
Global health community	**Supports realization of an integrated approach to HIV/FP delivery, aligning donors and policy makers.** With calls for integrated solutions and an expanding HIV prevention product landscape, the DPP could attract funders interested in HIV and SRH innovations. Investing in the DPP will signal to governments, procurement agencies and implementers that MPTs are a priority.	**Constrained funding envelope with reduced resources available for FP and HIV prevention and concurrent rollouts of CAB-LA and the ring may limit investment.** Leveraging funding opportunities for implementation research to offer multiple products will streamline investments and potentially save costs. Reassure the FP community and women that promoting an OC will not jeopardize progress on long-acting methods and that the added cost of ARVs will not erect novel access barriers.

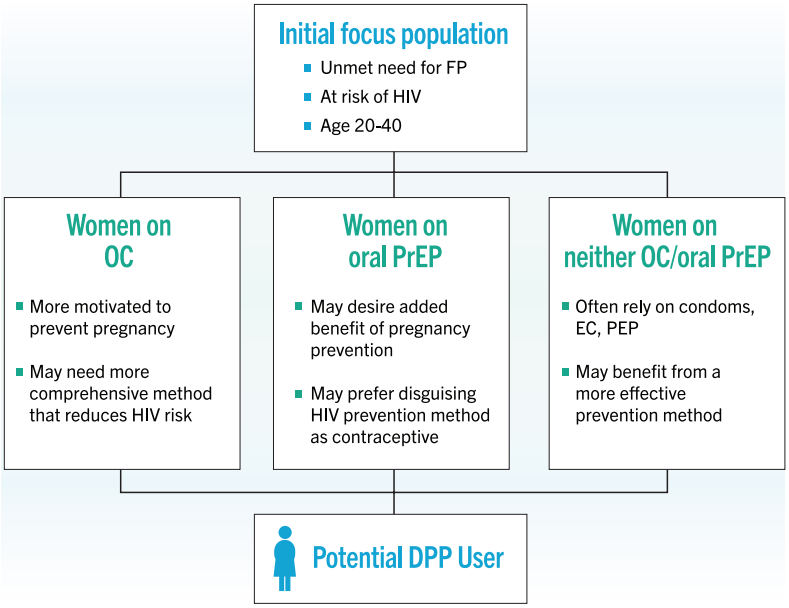
Figure 4: What does success look like for the DPP?



2. The user

Based on an initial analysis in multiple countries and HCD research in South Africa and Zimbabwe, **the recommended initial target population for DPP introduction is women ages 20-40**, as they have higher rates of OC/oral PrEP uptake and effective use of oral PrEP,[9] making them more likely to be early adopters compared to adolescent girls younger than 20 years. While older women are generally at lower risk of HIV acquisition, sub-national targeting will focus on DPP users in high-burden settings.[10] Pending regulatory approval, the indicated population will likely be all women of reproductive age. Developing varied approaches to reach women based on age brackets (e.g., ages 20-24, 25-29, 30-35) will help align outreach with different phases in their lives. Policy makers will ultimately make decisions on priority populations at country level.

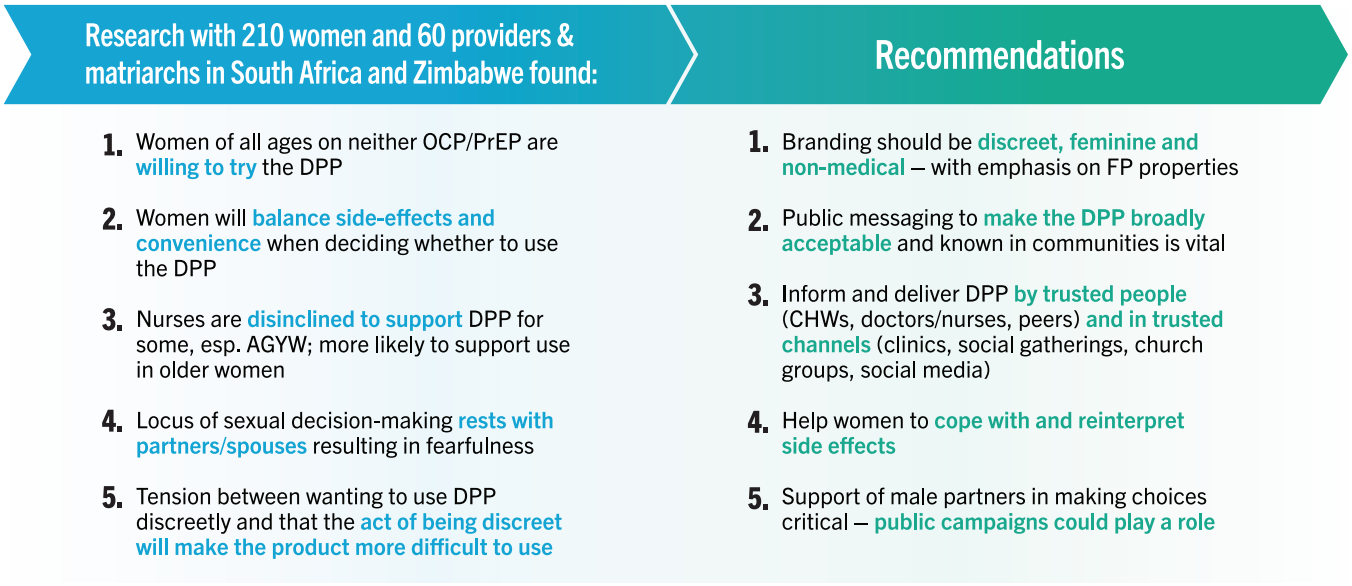
Figure 5: DPP Initial Focus User Profiles



Among women ages 20-40, early adopters are expected to be **urban women with higher income and OC and/or oral PrEP experience**, given profiles of current users of OC/oral PrEP and findings from end-user research on the DPP. Women who do not intend to conceive and who use emergency contraception (EC) and post-exposure prophylaxis (PEP) could also benefit from the DPP. Women on LARCs will not be encouraged to switch from more effective contraception, and should be offered oral PrEP, CAB-LA or, for women who are unable or do not want to take oral PrEP, the ring for HIV prevention.[11]

HCD research conducted with 210 end users and 60 providers and matriarchs in South Africa and Zimbabwe[12] found that most women expressed interest in using the DPP, with slightly higher interest among women living in urban areas. Primary concerns were: 1) side effects, as some women questioned whether a combined pill would have double or more intense side effects; and 2) ability to disguise the product from their partner – a finding more prevalent in Zimbabwe. In South Africa, especially among Women who have used neither OC or oral PrEP (OC- and oral PrEP-naïve) were motivated by the high incidence of rape to remain safe and protected amid a reality marked by gender-based violence.

Figure 6: Key findings and recommendations from HCD research in South Africa and Zimbabwe



In addition to the initial target population described, governments could consider prioritizing other groups of women based on country context, epidemiological trends and existing programs, which are more likely to require tailored outreach strategies:

- **Adolescent girls**: While they have a particularly high HIV risk and incidence,[13] lessons from oral PrEP roll-out and OC use suggest lower uptake.[14] Existing AGYW-specific initiatives (e.g., PEPFAR's DREAMS program,[15] the Government of South Africa's She Conquers campaign,[16] Global Fund's HER initiative[17]) and adolescent-friendly services should be leveraged to reach adolescent girls.
- **Female sex workers (FSW)**: The DPP aligns with FSW need for HIV and pregnancy prevention, and could be integrated at targeted delivery points through existing funding (e.g., Global Fund's catalytic funding for key populations programs[18]) and peer-led and FSW outreach programs.
- **Postpartum women**: Postpartum women in sub-Saharan Africa (SSA) are likely to have another child within 2-3 years[19] and may be drawn to a method with a shorter return to fertility. While COC (and thus the DPP) is not advised until 6 months postpartum, postpartum visits are an entry point for FP counseling. The DPP may be appealing given high HIV incidence in this period.[20]

III. Our Approach

This section outlines the strategic approach that the DPP Consortium will pursue to plan for, introduce and scale the DPP in prioritized countries, beginning with an overview of the process followed by proposed approaches in thematic areas along the research-to-rollout framework.

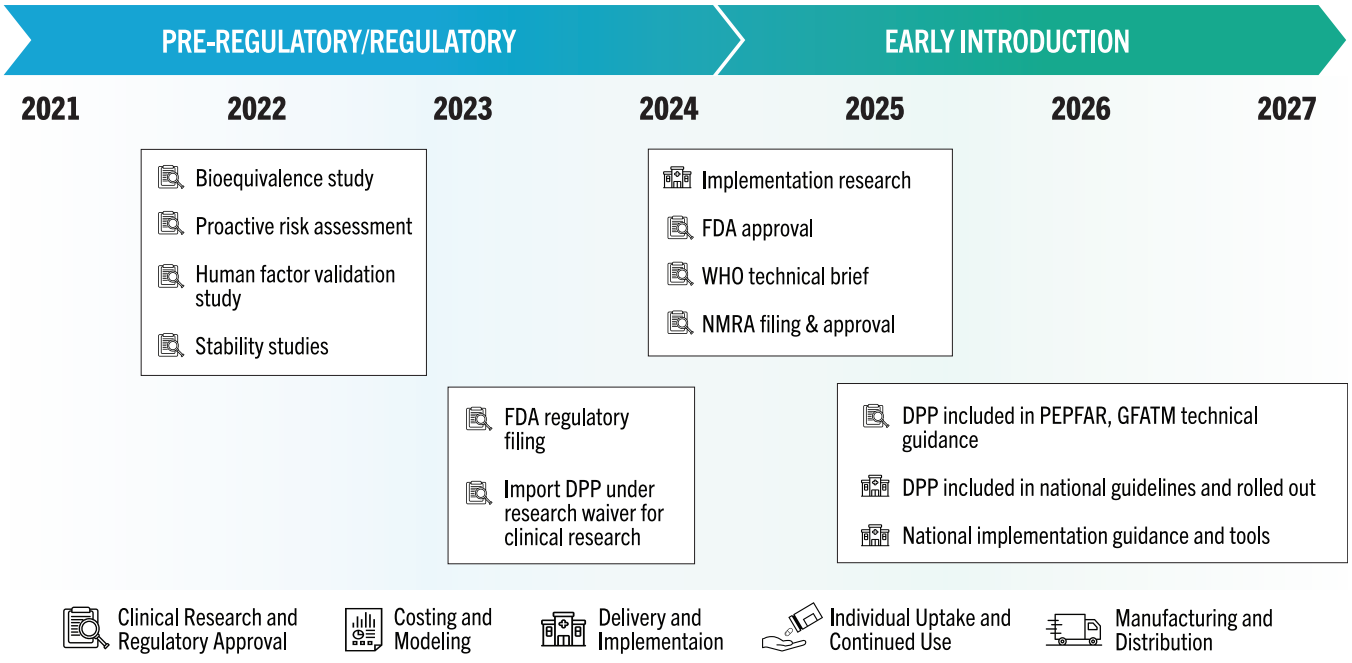
Recommended DPP regulatory and introduction pathway

1. Regulatory approvals and policies

From 2021-2022, prior to FDA submission, Viatris will conduct a bioequivalence (BE) study to assess the DPP's equivalence compared to oral PrEP and COC alone. A proactive risk assessment, including a comprehensive, systematic evaluation of steps involved in using DPP, and a human factor validation study are also likely to be conducted per an FDA requirement to understand potential user errors.

Viatris aims to file for regulatory approval with the US FDA in 2023 using a standard generic review pathway. Providing strong evidence to support DPP approval in lieu of a trial and early, extensive engagement with regulators and countries could accelerate time to rollout. Prior to or in parallel with FDA review, implementation partners can pursue IRB approval and import the DPP under a research waiver to be used in implementation research[iii] to speed real-world evidence generation, although permissions may vary by country. If funded and approved, clinical research (including acceptability studies using the co-formulated tablets) can likely start prior to FDA filing as long as the BE study is successful.

Figure 7: Regulatory pathway for the DPP



iii The terms "implementation research" and "demonstration project" are often used interchangeably. We use "implementation research" throughout this strategy, and nomenclature will be agreed upon as the project evolves.

Once approved by the FDA, projected for 2024, Viatris will pursue approval directly with multiple national medicines regulatory authorities (NMRAs) (the WHO Collaborative Registration Procedure is unlikely). In some countries, it may be possible to file with NMRAs while the FDA review is underway. Based on initial country landscape analyses, NMRAs in Kenya, South Africa and Zimbabwe are likely to allow for the BE of a fixed-dose combination product to be compared with the individual components of the product, as long as co-formulation of the two single-entity products is clinically justifiable under local regulations. A regulatory forum is planned in 2022 to better understand regulatory processes with NMRAs.

In late 2024 or early 2025, the DPP Consortium will support the World Health Organization (WHO) to pursue an expedited review process for inclusion in global normative guidance, as the DPP is not an innovator product and thus will not require specific guidelines. When positive BE study results are available, the data, along with findings on user values and preferences from acceptability studies, consultations and any published research on the DPP, will be reviewed to issue a technical brief (similar to the approach with event-driven oral PrEP and the ring[21]). For the ring, the process from EMA opinion to WHO pre-qualification (PQ) took five months and was aided by strong backing from key stakeholders. WHO's recommendation of the dapivirine vaginal ring as one HIV prevention option for women at substantial risk for HIV acquisition was published three months after PQ. These are possible benchmarks for the WHO's review timeline, assuming the DPP has sufficient support from funders and the scientific community.

By 2026, positive BE results, stringent regulatory approval, acceptability studies, implementation research and WHO PQ will provide the impetus for inclusion in PEPFAR guidance and revisions to national guidelines. At country level, context-specific evidence on acceptability and impact modeling will accelerate funding allocations and inclusion in guidelines. A national coordination mechanism, likely established with country-level technical assistance and comprised of SRH and HIV prevention stakeholders including experienced end users, should review evidence and steer the guideline revision process, in alignment with other new HIV prevention products. Pilot studies will provide further evidence on cost-effectiveness, FP and HIV outcomes, demand and effective messaging to inform national implementation guidance and tools.

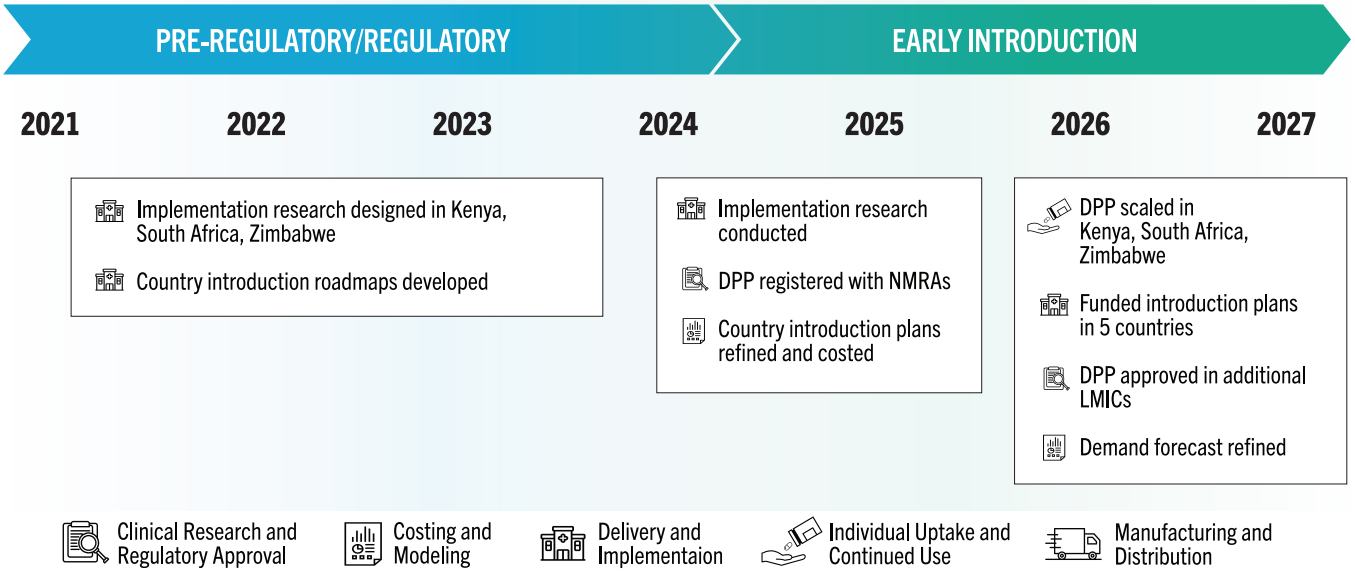
2. Regulatory review and early introduction

The DPP will be rolled out in a phased, evidence-driven process in countries that demonstrate interest and readiness to introduce the DPP and high potential for impact. Early introduction countries will be able to quickly build regional evidence, contingent on available funding.

Three countries have prioritized plans to design initial implementation research and undertake introduction planning in 2021-2023. Early evidence for scale-up will be generated in Kenya, South Africa and Zimbabwe, which were prioritized based on a scoping of **need** (identified as high HIV incidence and high unmet need for modern contraception, with geographic overlap of both); **potential demand** (indicated by high OC use) and **enabling environment** (defined by existing PrEP policies and investments allocated to scale national PrEP programs). More countries could be added with additional interest and funding commitments.

Governments, through existing technical working groups (TWGs) or other national coordination mechanisms, will develop country introduction roadmaps with support from the DPP Consortium if needed. Roadmaps should include sub-national target-setting, prioritized service delivery channels and pre-regulatory adaptations. Recent oral PrEP decision-making (e.g., in South Africa) indicates that with technical assistance to support sub-national target-setting, the DPP could quickly scale. Assessment criteria for sub-national targets should look at: (1) high unmet need for FP and high HIV prevalence (and/or incidence where measured); (2) high OC use and high potential for total addressable market for contraception (TAMC) and (3) PEPFAR DREAMS districts, given high need, engagement of women ages 20-24 and linkages to SRH services.[22]

Figure 8: Regulatory review and early introduction of the DPP

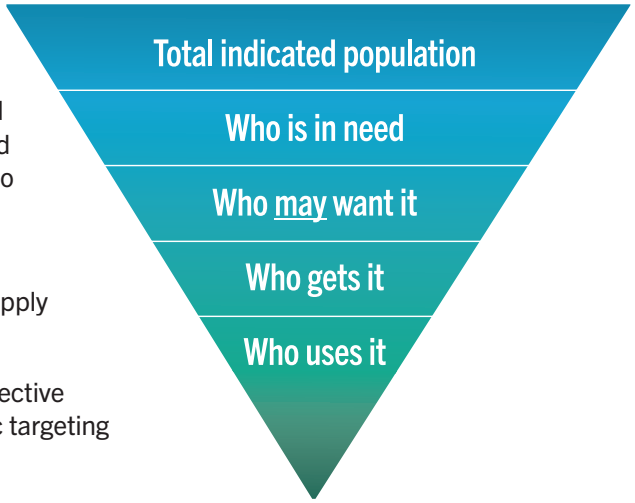


Implementation research is expected to begin by 2024 to rigorously assess acceptability, impact, cost-effectiveness and feasibility to deliver the DPP in different service delivery channels in Kenya, South Africa and Zimbabwe. The DPP Consortium will recommend additional countries for prioritization and partners will work with governments to support adoption of favorable policies, cost-effectiveness studies, target-setting, costing introduction plans and other critical activities, building the DPP into existing delivery platforms as feasible. With additional donor resources and favorable outcomes from implementation research, other countries that meet introduction criteria could roll out the DPP.

By 2026, the DPP should be scaled in Kenya, South Africa and Zimbabwe – assuming implementation research shows evidence of impact – with the goal of having funded introduction plans in at least 5 countries and regulatory approvals in additional countries. A preliminary analysis estimates 15 countries in SSA with HIV prevalence rates greater than 3% among women 15-49 have a potential total available market of 250,000-1.25 million DPP users per year. However, these estimates do not factor in potential discontinuation rates, anticipated growth in the oral PrEP market given oral PrEP targets, and ring and CAB-LA introduction. To hone this initial estimate to identify the target market, an **evidence-based demand forecast for the DPP will be developed alongside other evolving HIV and FP product forecasts and will be continually refined** based on:

- **Who needs it?** The total indicated population will be narrowed to identify who is in need of the DPP based on disease burden, risk profile and unmet needs.
- **Who may want it?** Ahead of introduction, based on planned end-user research and data from acceptability studies, need estimates can be refined to provide an initial estimate of who may adopt, via new use or conversion, the DPP.
- **Who gets it?** During early introduction, an uptake curve or demand forecast can be estimated based on clinical and supply considerations, implementation planning and user trends.
- **Who uses it?** Data on user characteristics, initiation and effective use will refine the demand forecast and steer programmatic targeting toward particular populations and service delivery settings.

Figure 9: Progressive demand forecast for the DPP



3. Implementation evidence generation

Implementation research will be designed in collaboration with governments and in consultation with advocates, end users, researchers, professional associations and other key stakeholders. It will initially be conducted in Kenya, South Africa and Zimbabwe, likely in public sector FP and HIV service delivery points, across urban and rural settings and among different segments of women, with aligned research protocols to allow meta-analysis and evaluate acceptability, impact, cost-effectiveness and feasibility. Private sector channels may be considered, contigent on authorization to prescribe oral PrEP in these settings. Funding opportunities across donors will be leveraged to pursue choice-based studies that offer the DPP with oral PrEP, CAB-LA and the ring to provide a nuanced understanding of user preferences in real-world settings.

Primary implementation research partners will have track records of rigorous implementation research on HIV prevention and SRH, strong government and civil society relationships, established presence and reach in-country and across settings and experience with oral PrEP and FP introduction and delivering HIV and SRH services. Potential advocacy partners will include local advocacy organizations in Kenya, South Africa and Zimbabwe as well as regional advocacy coalitions, such as the Civil Society Advocacy Working Group on Hormonal Contraception (HC)-HIV. Civil society advocates, other community representatives and potential end users will contribute to shaping research engagement with women and communities. They will help build literacy, communicate results and advise governments and donors on implementation priorities to ensure community voices are represented through research and rollout. Advocates will raise awareness on and mobilize support for HIV prevention broadly as well as product-specific activities, including for the DPP, CAB-LA and the ring. Other partners (e.g., private sector, community-based women's groups) may be incorporated as the project evolves.

Research objectives are outlined in the following table. **Sub-studies will be conducted to inform scale-up** on cost/cost-effectiveness, utilization in different delivery channels, demand generation and provider motivators and barriers. Sub-studies on other objectives may be implemented with additional resources. Findings from implementation research will be used to influence national policies and scale-up, including around regulatory re-classification of PrEP to expand access, and to provide evidence for DPP rollout in other countries.

Figure 10: Primary and secondary research objectives for implementation research

Primary objectives	Secondary objectives
■ **Clinical outcomes** of the DPP (e.g., sero-conversions, pregnancy, adverse events, STI incidence). ■ DPP **initiation/effective use** across sites, channel types, other FP/HIV prevention methods, different segments of women. ■ **Provider motivators or barriers** to offering the DPP to a client. ■ **Cost/cost-effectiveness** of delivering the DPP in each setting. ■ **Optimal positioning** of the DPP vs. other FP/HIV prevention methods. ■ Impact of DPP introduction on **advancing HIV/SRH integration**.	■ **Strengthened platforms and lessons generated** for future MPT introduction. ■ **Characteristics and preferences** of women that initiate the DPP in each setting, including demographics and barriers/motivators to initiation. ■ Common **reasons for discontinuation or switching**, and support needed if HIV or pregnancy status changes. ■ **Training, supervision and other support** providers require to correctly deliver the DPP. ■ **Optimal clinic flow, mix of cadres, hours and areas of operation** to maximize client reach. ■ **Opportunities for task shifting** to lower-level providers and differentiated delivery approaches, such as HIV self-testing (HIVST).

4. Service delivery

Across countries, the DPP will be introduced and scaled in service delivery channels that have the greatest potential to reach women where they prefer to access services and are least stigmatized. Potential DPP channels were assessed based on: (1) alignment with user behaviors & preferences; (2) cost-effectiveness; (3) health systems readiness; (4) strength of M&E systems and (5) scalability.

The analysis found that **FP/MCH/SRH service delivery points** span client types and are a high-potential entry point for the DPP, as women are often introduced to FP (and to a lesser extent oral PrEP) in these settings through counseling, even if they are seeking other services, such as EC or post-abortion care. **HIV clinics and PrEP delivery points** are best equipped to deliver the DPP, where providers are already trained to provide ARVs, though associated stigma and limited relevance for women who may not be as motivated to actively seek HIV prevention – typically not a primary concern– may limit reach. While **private sector and innovative channels** (such as telehealth and mobile clinics) may not be as ready to scale, they are often preferred by specific user groups, and those permitted to provide PrEP should be considered for implementation research. The PrEP landscape is quickly evolving – with a shift toward simplified and differentiated delivery that both preceded and was amplified by COVID-19. **Additional channels should be considered for the DPP as soon as they are able to offer PrEP**.

a. Delivery channel selection in prioritized countries

An initial analysis recommends that implementation research in Kenya, South Africa and Zimbabwe be conducted in public FP and HIV clinics, followed by scale-up in high-potential channels outlined in Figure 10. As PrEP is decentralized, innovative and private channels with capacity to deliver PrEP and that have potential for impact and scale will be sequenced earlier. Governments will validate and ultimately determine channel sequencing in each country.

Figure 11: Service delivery channel sequencing in prioritized countries

Phase	Years	Channels	Rationale
1	2024-2025	■ Public FP/SRH clinics ■ Public HIV clinics	**High-capacity public sector channels** are most likely to be scaled and sustained after introduction.
2	2025-2026	■ Pharmacies ■ Social franchises/NGOs ■ DICEs/Population-specific sites ■ Mobile clinics	As a rapidly changing private sector expands the channels delivering PrEP, **Phase 2 channels show potential for impact**.
3	2026+	■ Private providers ■ Universities ■ Telehealth ■ Direct-to-consumer ■ CBD programs for FP	Phase 3 channels are some of the **most decentralized for OC, but require significant policy changes to offer PrEP or are in nascent stages of oral PrEP delivery**. As soon as these channels can offer PrEP, they should be elevated for the DPP, as they are most likely to respond to end users' needs and preferences. Simplifying PrEP delivery and enshrining task-shifting for PrEP in policy will thus be a priority for DPP market preparation.

An analysis of the private sector found user preferences are the impetus to introduce the DPP in pharmacies in Kenya and South Africa (in Zimbabwe, private sector introduction will not be prioritized). While financing will be tied to the rollout of national health insurance in both countries, pharmacy introduction will require subsidized commodities and tailored distribution models to support availability of an affordable product; platforms like Maisha Meds' Digital Pharmaceutical Benefits manager should be considered. Demand-side financing mechanisms such as technology-enabled voucher schemes can address affordability issues while targeting subsidies to those that require it. Advocacy is needed to support policy shifts that include task-shifting for HIV testing, prescribing and refilling for pharmacists.

Private sector models such as social marketing organizations and public-private partnerships (PPPs) should be engaged to negotiate product introduction in the private sector. These models will require technical support to address financing challenges, tailored distribution, monitoring and reporting solutions and training and support for providers (including counseling, referrals and linkages).[27]

DPP introduction will be expedited by pursuing channels that have integrated HIV/SRH services, task-shifted delivery of PrEP and already offer HIVST. In the pre-regulatory period, the DPP Consortium will work with countries to validate adaptations required for DPP delivery and link governments to appropriate, ongoing technical support in-country and through other co-investments. As the DPP moves closer to introduction, this strategy will be referenced to ensure delivery needs are addressed, including through existing investments in other HIV prevention products (CAB-LA; the ring).

For instance, strong national mechanisms will be leveraged to coordinate and improve integrated service delivery, such as the HIV/SRH integration sub-committee in Kenya, PrEP and AGYW TWGs in South Africa and PrEP and SRH TWGs in Zimbabwe. Kenya, South Africa and Zimbabwe have conducive policy environments for DPP rollout, but more work is needed to integrate HIV/SRH services and systems.[28] Innovative approaches, including youth-friendly sites and oral PrEP pilots in FP clinics, can inform capacitation of the public sector to take PrEP to scale.

b. Clinical/quality strategy

Facilitating DPP uptake and continued use will rest on closer alignment between requirements for initiating OC and oral PrEP given different instructions for use, different standards for client follow-up across FP and HIV prevention and that OC delivery points are more aligned with women's preferences. Planning for DPP introduction will thus require:

Moving toward OC requirements that are clinically acceptable and responsible for oral PrEP.

- **Further simplify and streamline testing** to ease clinical monitoring (e.g., refills every 3 months, HIV testing especially for initiation, STI self-sample collection and dropping creatinine testing requirements for younger people). HIV testing would follow national guidelines for PrEP prior to initiation, after 1 month and then every 3 months, which may be perceived as a barrier for current OC users, though changes to WHO guidelines on HIV testing could prompt loosening requirements for HIV testing at country level. Some oral PrEP implementation projects (e.g., POWER) are assessing the feasibility of using HIVST to reduce clinic visits;[29] evidence shows young women like and prefer HIVST,[30] and community and peer-led distribution of HIVST has worked in South Africa and Zimbabwe.[31]
- **Sustain user-friendly adaptations to oral PrEP and FP delivery** such as multi-month dispensing (MMD), online follow-up and monitoring, task-shifting to lower-level provider cadres, HIVST and peer-led or assisted outreach, testing and adherence support — delivered closer to home. MMD should be offered after the first month where permitted. Distributing OC packs — and more of them — is associated with higher rates of effective use compared to OC prescriptions with more frequent return visits.[32] MMD for oral PrEP and OC has been implemented in many countries due to COVID-19 and should be sustained.[33] Making it easier for women to obtain the DPP across sites and channels, including via self-care platforms, and reducing clinic visits recognizes that some women are highly mobile and may access services at different delivery points.

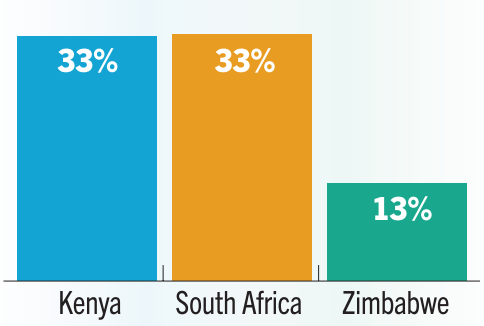
Ensuring a high quality of initial counseling on the DPP. A provider counseling sub-group, comprised of global clinical experts with country-level expertise in HIV and SRH, will develop initial counseling guidance messages to be tested in acceptability studies. Messaging and related tools will be adapted to the needs of other channels, including pharmacies and social franchises supporting the private sector.

- **Providers must be equipped to support users to understand the product and benefits**, while decreasing the cognitive load of learning about two products at once. Providers must situate the DPP – a new product – within a range of prevention options and uphold informed choice.
- **Providers must be trained to support women through the pathway to care**, including screening and HIV testing, counseling, referrals for those that test positive for HIV and reporting. Initially, training and supervision may be funded and supported by donors and implementing partners. Longer term, technical support supervision for providers will transition to governments overseeing more diversified and integrated prevention programs.
- **Providers should be able to support women to anticipate and cope with side effects**, one of the most common reasons women stop using both OC and oral PrEP. Explaining potential side effects and how to manage them – without overemphasizing them – will be key. This includes menstrual bleeding/spotting issues from irregular pill-taking, a known concern for women.
- **Providers should spend time discussing potential for pausing, switching or restarting** – for instance, if a woman's fertility intention changes, if she dislikes the DPP but still needs dual protection or if her relationship status changes or induces a desire to discontinue her current method.

Establishing a level of support for follow-up, including use of peer outreach and mHealth. Acceptability studies and implementation research will offer insights on end-user preferences and successful approaches for follow-up.

- **Women that discontinue or switch** methods as fertility intention or risk change will require more support than typically provided in FP programs. Discontinuation is common among OC[34] and oral PrEP[35] users. Decision support tools have been developed to support informed choice for FP methods and as self-assessment tools for oral PrEP initiation. Implementing partners are revising these tools as more HIV prevention options become available. The DPP should be integrated into both FP and PrEP decision making tools, which could help women to assess which method would work best for them.[36]
- **Identify the level of follow-up required** if a client does not return for a refill based on counseling and any barriers to access that may have been discussed. FP and HIV approaches diverge, with FP taking a more passive approach and the majority of clients discontinuing a method on their own. Oral PrEP and ART follow-up tends to be more proactive and resource-intensive.
- **Level of follow-up should be as close to FP support as possible to minimize provider and client burden** while building on existing HIV infrastructure and successful oral PrEP support interventions, such as peer outreach and mHealth.[37] These include early identification of women who may be at greater risk of discontinuing, contacting women who miss a refill or digital reminders to take pills, which could also help identify those inclined to discontinue the DPP. This may be a new experience for oral PrEP-naïve users, requiring explaining upfront.
- **Integrate the DPP into existing mHealth applications** – outreach, educational and counseling messages, decision support tools and reminders for refills via mobile phones – which are effective at keeping women engaged in FP and HIV services.[38]

Figure 12: Annual discontinuation rates of OC while in need



FP2020 Core Indicator Summary Sheet: 2019-2020 Annual Progress Reports for Kenya, Zimbabwe; South Africa Demographic and Health Survey 2016.

c. Provider training/provider demand generation

Based on a review of policies on oral PrEP and FP provision, nurses are currently the lowest level cadre with the highest workforce coverage eligible to prescribe and dispense the DPP across prioritized countries.[39] FP nurses will need training on oral PrEP and may require support to manage additional burden to their workloads. ART/PrEP-certified nurses may need refresher training on FP and training on how to counsel and support women to use a combined product. Qualified cadres in the private sector will need to be integrated into training programs targeting public providers. To maximize delivery and preempt stigma around the DPP, providers and governments should:

Advocate for policy changes and support expanded trainings to task-shift PrEP delivery to pharmacists, community health workers (CHWs) and other cadres, supporting efforts that are underway to align with OC provision and expand viable DPP service delivery points. Advocacy partners must be sufficiently funded as their engagement with government decision-makers is critical for designing prevention programs that best serve users and communities.

Support women to use self-testing for HIV and pregnancy, including via co-delivery of self-test kits, and capacitate peer navigators/lay workers to do testing, counseling and referrals to offset provider workloads, especially in large tertiary hospitals.

Incorporate provider-focused behavior change interventions into clinical training, as nurses may be disinclined to support the DPP for younger women, who they believe cannot be trusted to take daily oral pills, but would support the DPP for older women, who they see as more responsible and who may want the flexibility of an OC.[40] Poor product knowledge of oral PrEP among providers, particularly in Zimbabwe, is an added barrier – oral PrEP scale-up can begin to build their literacy now. [41] Values clarification training has been successfully employed to address provider bias.[42]

Adapt clinical mentorship programs and provider communities of practice to support provision of the DPP. Mentor models/champions have helped build provider capacity to deliver oral PrEP and FP.[43]

5. Promotion/demand generation

a. Branding the product

Building off the oral PrEP experience and a range of HCD and market research, **the DPP will be branded with a lifestyle feel**, as a product women can integrate into their daily routines.[44] HCD research on the DPP found that women want branding and packaging to be discreet, feminine and non-medical, with no obvious references to HIV or oral PrEP, as perceived association with HIV is stigmatizing and will likely dissuade use. Women respond positively to branding that feels relevant and familiar, and products that instill confidence and self-efficacy.

Viatris is opting for a wallet-pack structure for the DPP with sheets that tear off a week of blister-packed pills, which will more closely resemble OC packs. This decision responds to an aversion to products that look like oral PrEP or ARVs and that are less discreet, such as pill bottles. Viatris has developed and vetted potential brand names based on regulatory requirements, and a marketing firm will conduct research with end users to inform the decision for a brand name that resonates globally. Focus groups will be engaged to assess women's viewpoints and preferences to ensure that the design reflects their inputs.

b. Demand generation strategy/community engagement

Early on, oral PrEP programs did not adequately invest in demand generation strategies, which contributed to low public awareness and acceptance. HCD research conducted in South Africa and Zimbabwe found that women's most important ask for the DPP is: **"Help us to not have to be discreet."**[45] Women acknowledged that the DPP could bring self-confidence but feel they need help to overcome disempowerment in relationships. **Making HIV prevention and contraception use (and the DPP specifically where marketing regulations allow) "popular" through public messaging and endorsement can create social acceptability**, which could help eliminate men's mistrust of OC/oral

PrEP by promoting the shared benefits of the product. **Messaging geared toward women should allay fears (e.g., of side effects) and position HIV and pregnancy prevention as a convenient choice** that can reduce stress and fear of potentially undesired consequences of sex.

HCD research findings and a review of evidence on demand generation for oral PrEP and OC highlight key elements for a demand generation strategy for the DPP. AVAC and Population Council will validate findings from HCD and formative research with country-level stakeholders, and insights will be used to design campaign briefs for implementation research in 2022-2023.

6. M&E

Given significant variability between oral PrEP & OC program measurement, it will be crucial to drive an early consensus on critical and enabling DPP indicators. Current usage and impact of oral PrEP can be estimated with: (1) new initiations; (2) return for first follow-up visit and (3) current clients, if those indicators are collected and data is available at that level of disaggregation. FP usage estimates are generally extrapolated from commodity distribution (HMIS, LMIS) and global and national surveys (UNFPA facility, PMA, DHS): (1) stockouts; (2) couple-years protection and (3) method availability.

Global and country consultation groups of HIV prevention and FP implementers, MOH representatives, normative agencies and researchers should be convened to draft guidance to define initial best practices for DPP M&E. Systems will need to be updated and aligned to collect and disaggregate information. While DPP indicators will ultimately be included at the discretion of national governments and major bodies such as the WHO and PEPFAR, this **DPP global consultation group will provide recommendations on:**

- **Critical indicators** for target-setting, impact measurement and clinical monitoring across HIV prevention and FP programs, including opportunities for integration
- **Enabling indicators** or demographic information to refine demand generation and programmatic approaches – "nice-to-haves" that will need to be calibrated with the added burden to collect them on top of critical indicators

To help speed up inclusion in M&E systems, the DPP Consortium will work through complementary projects to **support country efforts to strengthen and align national M&E systems across HIV and FP programs**, with a move toward electronic monitoring systems, prior to DPP rollout. Importantly, these efforts should establish best practices and update protocols to accelerate inclusion of future MPTs.

7. Supply Chain

The current manufacturing capacity is expected to be sufficient for at least the first three years. Viatris is expected to be able to produce a supply for 250,000+ women per year, and may be able to increase capacity further with additional packaging equipment. As demand becomes clearer, needed capacity will be reassessed and additional manufacturers may need to be engaged to enter the market to increase supply and enable scale. LNG/EE can only be manufactured in dedicated hormonal facilities, so ideal manufacturers will already be manufacturing an LNG/EE OC product.

While the cost of the DPP compared to other HIV prevention and FP options suggests that the product will likely be procured primarily by HIV-focused agencies, success will require delivery in public sector FP programs and via private sector partnerships. This will require early, extensive coordination to align separate HIV/FP target-setting, quantification, procurement plans, funders and intervention costs at country level. Though some HIV donors, such as PEPFAR, have not purchased contraceptives to date, the DPP may be an opportunity to explore this.

Global procurement for the DPP will thus be best supported by assessing opportunities to integrate HIV prevention products and MPTs into existing global coordination mechanisms, such as the ARV Procurement Working Group (APWG), which facilitates coordinated procurement of low-volume products through quarterly order placement

cycles. With multiple new products heading to market, including CAB-LA and the ring, it is likely that a **new Prevention Procurement Working Group could become a sub-group of the APWG.** As the DPP progresses, engaging key FP stakeholders, such as the Reproductive Health Supplies Coalition, FP2030 and UNFPA, would benefit DPP procurement and establish a coordination platform for future MPTs.

National procurement and planning processes will require tailored strategies for engagement.[46] For HIV commodities, South Africa contributes significantly to funding and is now the largest procurer of condoms in the world,[47] whereas Kenya and Zimbabwe rely more on donor funds. National supply chain management systems and public sector supply chain agencies will need to bridge traditional HIV and FP channels to ensure the DPP and ancillary products, such as HIV testing (in FP clinics) and pregnancy tests (in HIV clinics), can be reliably supplied to prioritized distribution points. As HIV and FP commodities are procured through separate supply chains in many countries, it will be crucial to begin supporting integration through targeted technical assistance in advance of product availability. Measures will need to be put in place to guarantee women uninterrupted access to OC/FP and oral PrEP as a stopgap in the event of a DPP stockout.

IV. Funding required and financials

1. Initial introduction

a. Cost estimate

The DPP will be advantageously positioned to scale if the cost is at parity with the combined cost of oral PrEP and COC, or, ideally, even lower. The current cost of generic daily oral PrEP is approximately $54/year, while the cost of daily COC is about $4/year. Based on an initial cost of goods (COG) analysis conducted by CHAI as part of the DPP Consortium, it may be feasible for the DPP to enter the market at parity with or lower than the cost of oral PrEP. This analysis will be refined as more data becomes available.

b. Initial value for money estimate

HIV funders may be encouraged to invest in the DPP if cost-effectiveness and end-user preferences are clear, especially given the anticipated simultaneous introduction of the ring and CAB-LA in locations where injectable contraception tends to be prioritized by many programs, providers and users. In advance of more rigorous cost-effectiveness modeling, **an initial value for money analysis of high-level DPP-related cost and impact outcomes will inform continued and co-investment for DPP introduction planning**. The analysis estimates directional financial savings from product co-formulation and service delivery integration as well as unintended pregnancies and primary HIV infections averted over a one-year snapshot of DPP use at a set number of annual users. The analysis does not include product introduction and start-up costs such as initial training or system changes, model costs or impact over multiple years, estimate secondary and tertiary HIV infections averted or examine detailed cost-effectiveness outcomes. Additional cost savings from avoiding lifelong ART and HIV labs and unintended pregnancies are an "additional upside" but were not included in the analysis.

While the initial value for money analysis provides an estimate of directional financial savings, inputs and assumptions, including (1) adherence to PrEP; (2) adherence to OCs; (3) DPP adherence; (4) commodity cost reduction at scale and (5) personnel cost reductions are expected to vary by country and will heavily shape the outputs of this analysis. **Impact estimates** assess unintended pregnancies and primary HIV infections averted. For HIV prevention, ensuring access for women who are at high risk of infection (based on estimated HIV incidence) and supporting adherence

through counseling and outreach will increase the impact of the DPP. With improved adherence and messaging about the enhanced benefits of a dual product, the DPP may have more impact on preventing unintended pregnancies. **Cost savings** estimates suggest that even with modest decreases in cost as compared to the individual products (i.e., DPP parity with oral PrEP), the **primary driver of direct cost savings will be reduced commodity costs due to co-formulation at scale**. Additional marginal savings may be gained due to integrated delivery of HIV and SRH services. The analysis does not account for product introduction and start-up costs, such as initial training and system changes; these costs will likely decrease overall savings.

c. Cost-effectiveness methodology

CHAI will define the preliminary methodology to model impact and costs of DPP introduction across HIV and pregnancy endpoints and articulate potential considerations for further comparative modeling. This framework will help inform more rigorous cost-effectiveness and impact modeling, which estimates the health outcome impacts of the DPP over time and in the presence of other programmatic and epidemiological factors, and will ultimately inform DPP adoption and procurement.

This process will also inform quantitative metrics to include in implementation research to further build evidence for government and donor investment decisions. This may include evidence around improved comparative uptake and adherence, comparative cost-effectiveness among new and continuing users and delivery cost efficiencies. Research will evaluate introduction across delivery channels, balancing end-user preference and impact with cost.

d. Financing

Funding for the DPP is likely to derive from existing HIV prevention budgets. In 2018, donors provided $38 million of global oral PrEP funding, of which $17.5 million (46%) was financed by PEPFAR (by 2020, PEPFAR allocated $35.7 million to PrEP; the total global funding for that year is not yet available).[49] The Global Fund is expanding its remit to include support for broader SRH interventions, and could be a funding source for the DPP. HIV care and treatment has taken a growing piece of the absolute budget for HIV funding, driven by the cost to support ever larger numbers of people enrolled on ARVs. Consequently, a growing number of HIV prevention interventions are vying for a shrinking piece of the funding pie.

While domestic financing is expected to remain low, there is a growing pressure for countries to finance the procurement of FP commodities. The South African government, which manages the largest national HIV response in the world and covers 75% of resource needs through domestic funding, could potentially finance the DPP.

FP donors may provide some degree of underlying infrastructure and service delivery funding, but are unlikely to pick up the substantively higher cost of oral PrEP in order to offer the DPP, especially in the current context of a shrinking FP funding landscape.

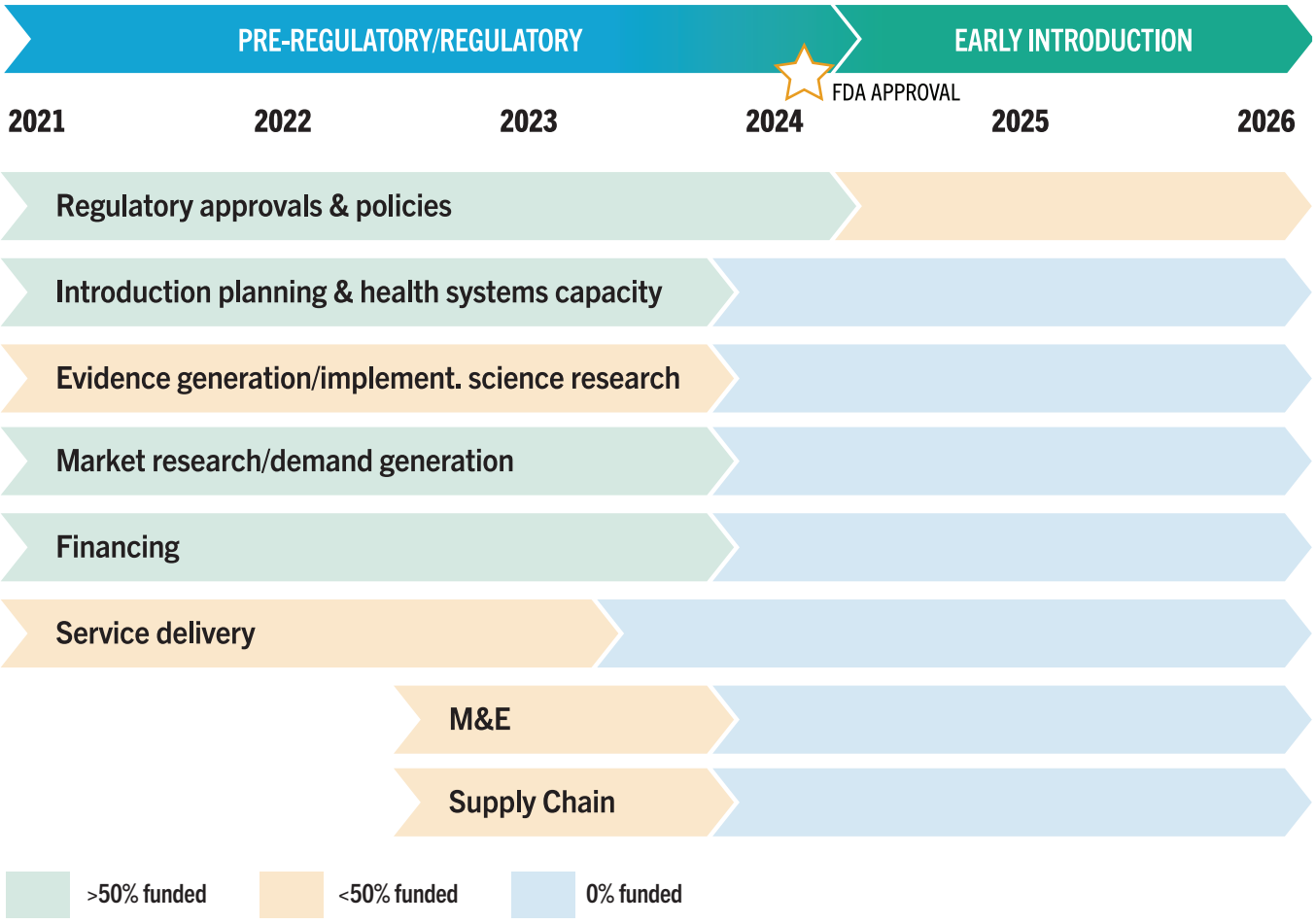
User willingness to pay will be low given oral PrEP is currently distributed for free, and generic OCs are affordable for much of the population. Introduction of the DPP into the private sector will require subsidization of the DPP to near-parity with OC, which will set the pricing bar for consumers.

2. Critical introduction activities

From 2021-2026, activities across the research-to-rollout framework will be critical to facilitate rollout of and access to the DPP. Based on initial cost estimates of market preparation and introduction activities, **approximately 61% have confirmed funding**, with other activities leveraging existing or anticipated co-investments. These cost estimates do not include investments in product development. Evidence generation/implementation science research activities are pending funding decisions that would cover design and implementation of research as well as sub-studies, provider training and related needs. While a significant portion of funding for pre-regulatory/regulatory activities has been secured, as of this writing early introduction activities are primarily unfunded.

The graphic below is a high-level snapshot of the approximate funding status of activity categories, which bundle the activities described in the preceding sections of this document. The table will serve as a reference when coordinating investments and tracking activity progress, including opportunities to integrate with or leverage complementary projects to fulfill needs.

Figure 13: Estimated funding for critical introduction activities for the DPP



V. Annex

1. List of Acronyms

AGYW	Adolescent girls and young women	**LNG/EE**	Levonorgestrel and ethinyl estradiol
APWG	ARV Procurement Working Group	**M&E**	Monitoring and evaluation
ART	Antiretroviral treatment	**MCH**	Maternal and child health
ARV	Antiretroviral	**MMD**	Multi-month dispensing
BE	Bioequivalence	**MPT**	Multipurpose prevention technology
CAB-LA	Long-acting cabotegravir	**NGO**	Non-governmental organization
CBD	Community-based distribution	**NMRA**	National medicines regulatory authority
CHAI	Clinton Health Access Initiative	**OC**	Oral contraception
CHW	Community health worker	**Oral PrEP**	Oral pre-exposure prophylaxis
CIFF	Children's Investment Fund Foundation	**PEP**	Post-exposure prophylaxis
COC	Combined oral contraception	**PPP**	Public-private partnership
COG	Cost of goods	**PQ**	Pre-qualification
DICE	Drop-in center	**PrEP**	Pre-exposure prophylaxis (all delivery forms)
DPP	Dual Prevention Pill	**SRH**	Sexual and reproductive health
EC	Emergency contraception	**SSA**	Sub-Saharan Africa
FDA	U.S. Food & Drug Administration	**STI**	Sexually transmitted infection
FP	Family planning	**TAMC**	Total addressable market for contraception
FSW	Female sex worker	**TDF/FTC**	Tenofovir disoproxil fumarate with emtricitabine
HCD	Human-centered design	**TWG**	Technical working group
HIVST	HIV self-testing	**WHO**	World Health Organization
LARC	Long-acting reversible contraceptive		

2. Figures

Figure 14: Cross-country factors for DPP potential in SSA

Metric	Kenya	South Africa	Zimbabwe	Eswatini	Zambia	Botswana	Malawi	Uganda
HIV prevalence rate (15-49, all adults)[50]	4.2%	19.1%	11.9%	26.8%	11.1%	19.9%	8.1%	5.4%
Unmet need for FP (15-49, all women)[51]	12%	11%	8%	10%	15%	8%	13%	19%
OCP use (% of method mix)[52]	14.1%	10.5%	56.5%	6.6%	14.4%	4.9%	3.8%	5.5%
Year PrEP approved[53]	2015	2015	2017	2017	2017	2016	2017	2016
Oral PrEP initiations[54]	93,621	164,537	39,745	25,617	131,951	5,958	1,623	116,068
FP Effort Index[55] (strength of FP program)	49.4	60.8	58.7	52.3	43.9	-	47.6	51
Ring intro planned[56]	X	X	X	X	X		X	X
CAB-LA trial experience[57]	X	X	X	X		X	X	X
ECHO trial experience[58]	X	X		X	X			
PEPFAR priority country[59]	X	X	X	X	X	X	X	X
GFATM priority country[60]	X	X	X	X	X	X	X	X
UNFPA priority country[61]	X		X		X		X	X

Figure 15: DPP service delivery assessment criteria and prioritized channels most likely to be utilized by user group

	Service Delivery Channel	Alignment with User Behaviors & Preferences	Cost-Effectiveness	Health System Readiness	Strength of M&E Systems	Scalability	KENYA	SOUTH AFRICA	ZIMBABWE
Public	HIV Clinic						1	1	1
	FP Clinic						1	1	1
	DICE/Population-Specific Site						2	2	2
	Mobile Clinic						2	2	2
	CBD Program						X	X	3
Private	Pharmacist (1st re-supply)						2	2	2
	NGO Model/Social Franchising						2	2	X
	General Practitioner/ Private Provider						3	3	X
	University						X	3	3
	Direct-to-Consumer (D2C)						3	3	3
	Telehealth						3	3	3

High opportunity/ Low risk

Medium opportunity/ Medium risk

Low opportunity/High risk/Not enough info

**Numbers in country columns correspond to the phase recommended to introduce DPP in that channel. "X" signifies channel will not be prioritized.*

Figure 16: DPP service delivery channels most likely to be utilized by user group

Channels	Women (20-40)	Adolescent Girls (15-19)	FSW	Postpartum women	Women using EC/PEP
Public FP/SRH clinics	X	X	X	X	X
Public HIV clinics	X		X		X
Pharmacies	X			X	X
Social franchises/NGOs	X	X	X		
DICEs/Population-specific sites		X	X		
Mobile clinics	X	X	X		
Private providers	X			X	
Universities	X	X	X	X	X
Telehealth	X	X	X		
Direct-to-consumer	X				
CBD programs for FP	X	X			

3. Key Resources

To access key resources that have been referenced throughout this strategy and for the latest materials on the DPP, please visit: https://www.prepwatch.org/nextgen-prep/dual-prevention-pill/.

References

[1] DPP Consortium. (2021). *Developing and Introducing a Dual Prevention Pill: Oral PrEP & oral contraceptive for HIV and pregnancy prevention*. https://www.prepwatch.org/resource/developing-introducing-dpp/

[2] AVAC & Matchboxology. (2020). *Dual Prevention Pill, South Africa and Zimbabwe: Digging for Insights*. On file with AVAC.

[3] Quaife, M., Eakle, R., Cabrera Escobar, M. A. et al. (2018). Divergent Preferences for HIV Prevention: A Discrete Choice Experiment for Multipurpose HIV Prevention Products in South Africa. *Med Decis Making*, 38(1), 120-133. https://doi.org/10.1177/0272989X17729376

[4] RTI International. (2020). *Listening to Young Women in Kenya and South Africa to Inform Multipurpose "2-in-1" Products for HIV and Pregnancy Prevention*. https://www.prepwatch.org/resource/listening-young-women-mpt/

[5] Minnis, A., Etima, J., Shapley-Quinn M.K. et al. (2021). Heterosexual couples' preferences for dual-purpose prevention products for HIV and pregnancy prevention: the CUPID Study (MTN-045) in Uganda and Zimbabwe. *HIV R4P 2021*. https://programme.hivr4p.org/Abstract/Abstract/676

[6] AVAC. (2021). *Advocates' Guide to Multipurpose Prevention Technologies*. https://www.avac.org/resource/advocate%E2%80%99s-guide-multipurpose-prevention-technologies

[7] *See* HIV Prevention Market Manager (PMM). (2020). *Breaking the cycle of transmission: A human-centered approach to increase adoption and sustained use of HIV prevention among high-risk adolescent girls and young women (AGYW) in South Africa*. https://www.avac.org/sites/default/files/resource-files/Breaking_the_Cycle_AGYW_SA_Oct_2020.pdf

[8] Quaife, M., Eakle, R., Cabrera Escobar, M. A. et al. (2018). Divergent Preferences for HIV Prevention: A Discrete Choice Experiment for Multipurpose HIV Prevention Products in South Africa. *Med Decis Making, 38*(1), 120-133. https://doi.org/10.1177/0272989X17729376

[9] See Mann Global Health. (2019). Kenya: Path-to-Market Analysis for the Dual Prevention Pill; South Africa: Path-to-Market Analysis for the Dual Prevention Pill; Zimbabwe: Path-to-Market Analysis for the Dual Prevention Pill. On file with AVAC. *See also*, e.g., Mugwanya K. K., Pintye, J., Kinuthia, J. et al. (2019). Integrating preexposure prophylaxis delivery in routine family planning clinics: A feasibility programmatic evaluation in Kenya. *PLoS Med 1*6(9), e1002885. https://doi.org/10.1371/journal.pmed.1002885

[10] UNAIDS. *AIDSInfo*. https://aidsinfo.unaids.org/

[11] World Health Organization (WHO). (2021). *Updated recommendations on HIV prevention, infant diagnosis, antiretroviral initiation and monitoring.* https://apps.who.int/iris/bitstream/handle/10665/340190/9789240022232-eng.pdf?sequence=1&isAllowed=y

[12] AVAC & Matchboxology. (2021). *Dual Prevention Pill: A Summary of Insights and Recommendations on the uptake of the combined PrEP and Oral Contraceptive pill by women of reproductive age in SA and Zimbabwe*. https://www.prepwatch.org/wp-content/uploads/2021/08/2021_07_30-End-user-findings-summary_public.pdf

[13] UNAIDS. *AIDSInfo*. https://aidsinfo.unaids.org/

[14] *See* Mann Global Health. (2019). Kenya: Path-to-Market Analysis for the Dual Prevention Pill; South Africa: Path-to-Market Analysis for the Dual Prevention Pill; Zimbabwe: Path-to-Market Analysis for the Dual Prevention Pill. On file with AVAC. *See also*, e.g., Mugwanya K. K., Pintye, J., Kinuthia, J. et al. (2019). Integrating preexposure prophylaxis delivery in routine family planning clinics: A feasibility programmatic evaluation in Kenya. *PLoS Med* 16(9), e1002885. https://doi.org/10.1371/journal.pmed.1002885

[15] U.S. Department of State. *DREAMS Partnership*. https://www.state.gov/pepfar-dreams-partnership/

[16] Government of South Africa. *She Conquers*. http://sheconquerssa.co.za/

[17] The Global Fund. *Women and Girls*. https://www.theglobalfund.org/en/women-girls/

[18] The Global Fund. *Key Populations*. https://www.theglobalfund.org/en/key-populations/

[19] Bietsch, K. (2019). *Healthy Birth Spacing Has Increased in Many sub-Saharan African Countries*. http://www.track20.org/download/pdf/Birth_Spacing_Memo_121719.pdf

[20] *See* Thomson, K. A., Hughes, J., Baeten, J. M. et al. (2018). Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners. *The Journal of Infectious Diseases 218*(1), 16-25. https://doi.org/10.1093/infdis/jiy113

[21] WHO. (2019). What's the 2+1+1? *Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: Update to WHO's recommendation on oral PrEP: Technical brief*. https://apps.who.int/iris/bitstream/handle/10665/325955/WHO-CDS-HIV-19.8-eng.pdf?ua=1; WHO. (2021, January 26). *WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women at substantial risk of HIV infection.* https://www.who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection

[22] *See* iMPT. *HIV Prevalence and Total Addressable Market for Contraceptives*. https://phi-cwn.maps.arcgis.com/apps/webappviewer/index.html?id=d6a43cc2587f41f0a11af7ba302e8745

[23] Begg, L., Brodsky, R., Friedland, B. et al. (2021). Estimating the market size for a dual prevention pill: adding contraception to pre-exposure prophylaxis (PrEP) to increase uptake. *BMJ Sexual & Reproductive Health, 47*(3), 166-172. https://doi.org/10.1136/bmjsrh-2020-200662

[24] EC use is common, especially among AGYW who tend toward event-driven rather than preventive behaviors. For instance, in Zimbabwe, 42% of 22-24 year-olds at tertiary institutions have used EC. Zimbabwe National Family Planning Council (ZNFPC). (2018). *Knowledge, Attitudes and Practices of Contraceptive Use among Students in Selected Universities in Zimbabwe.* http://www.znfpc.org.zw/wp-content/uploads/2020/06/Report-KAP-Study.pdf

[25] Maisha Meds. https://maishameds.org/

[26] Mann Global Health. (2020). *Private Sector Analysis for the DPP*. https://www.prepwatch.org/wp-content/uploads/2021/08/2021_07_30-SD-Strategy_Private-Sector-Analysis_public.pdf

[27] In Kenya, the Pharmacy-based PrEP initiation (PPI) implementation study is paving the way for pharmacy prescription and refills of PrEP, with oversight provided by a remote physician and prescriptions offered on rapid HIV test results. National Institutes of Health (NIH) RePORTER. *Pharmacy Delivery to Expand the Reach of PrEP in Kenya.* https://projectreporter.nih.gov/project_info_description.cfm?aid=9991948

[28] *See* PMM & Ministry of Health, Kenya. (2020). *Integration of HIV Prevention and Sexual Reproductive Health Services in Kenya.* https://www.avac.org/sites/default/files/resource-files/FP_HIV_integrationReportKenya.pdf; PMM & Ministry of Health and Child Care, Zimbabwe. (2020). *Integration of HIV prevention and SRH services in Zimbabwe*. https://www.avac.org/sites/default/files/resource-files/Zim_FP-HIV_integrationReport_July2020.pdf

[29] *See* Wanga V., Omollo, V., Bukusi, E. A. et al. (2020). Uptake and impact of facility-based HIV self-testing on PrEP delivery: a pilot study among young women in Kisumu, Kenya. *JIAS* 23(8), e25561. https://doi.org/10.1002/jia2.25561; ClinicalTrials.gov. *Kenya HIV Self-Testing in PrEP Delivery*. https://clinicaltrials.gov/ct2/show/NCT03593629

[30] Wanga V., Omollo, V., Bukusi, E. A. et al. (2020). Uptake and impact of facility-based HIV self-testing on PrEP delivery: a pilot study among young women in Kisumu, Kenya. *JIAS* 23(8), e25561. https://doi.org/10.1002/jia2.25561; Pettifor, A., Lippman, S. A., Kimaru, L. et al. (2020). HIV self-testing among young women in rural South Africa: A randomized controlled trial comparing clinic-based HIV testing to the choice of either clinic testing or HIV self-testing with secondary distribution to peers and partners. *EClinicalMedicine 21*, 100327. https://doi.org/10.1016/j.eclinm.2020.100327

[31] Shahmanesh, M., Mthiyane, N., Herbst, C. et al. (2021). Peer-distributed HIV self-test kits to increase demand for HIV prevention and care services in rural KwaZulu-Natal, South Africa: a three-armed cluster-randomised trial comparing social-networks versus direct delivery. *HIV R4P 2021*. https://programme.hivr4p.org/Abstract/Abstract/912; Sibanda, E. L., Neuman, M., Mangenah, C. et al. (2021). Comparison of community-led distribution of HIV self-tests kits with distribution by paid distributors: a cluster randomised trial in rural Zimbabwean communities. *HIV R4P 2021*. https://programme.hivr4p.org/Abstract/Abstract/828

[32] White, K. O., Westhoff, C. (2011). The effect of pack supply on oral contraceptive pill continuation: a randomized controlled trial. *Obstet Gynecol*, 118(3), 615-622. https://doi.org/10.1097/AOG.0b013e3182289eab

[33] *See*, e.g., Ministry of Health and Child Care, Zimbabwe. (2020, March 26). *Rapid Guidance on Service Delivery in the COVID-19 Context*. https://differentiatedservicedelivery.org/Portals/0/adam/Content/zzL5bQfq1EGMuHN3iyFoqw/File/ZIMBABWE%20-%20Rapid%20guidance%20on%20HIV%20Service%20Delivery%20in%20COVID-%2019%20%20CONTEXT%20-%20CORRECT%20DOCUMENT.pdf

[34] Most FP clients who switch to another method do so within 3 months of discontinuing.

[35] *See* Pintye, J., O'Malley, G., Kinuthia, J. et al. (2021). Influences on Early Discontinuation and Persistence of Daily Oral PrEP Use Among Kenyan Adolescent Girls and Young Women: A Qualitative Evaluation From a PrEP Implementation Program. *JAIDS*, 86(4), e83-e89. https://doi.org/10.1097/QAI.0000000000002587

[36] See Microbicide Product Introduction Initiative (MPii). (2017, September 13). *POWER – September 2017*. https://mpii.fhi360.org/power-september-2017

[37] Rodrigues, J., Mukoma, W., Reed, J. et al. (2021). Starting and staying on PrEP: a scoping review of strategies for supporting and improving effective use of PrEP. *HIV R4P 2021*. https://programme.hivr4p.org/Abstract/Abstract/1088

[38] PATH, AVAC & International AIDS Society. (2021). Bringing PrEP to the people: Democratizing access to PrEP through differentiated delivery before, during, and after COVID-19. *HIV R4P 2021*. https://programme.hivr4p.org/Programme/Session/57; OPTIONS Consortium. (2020, May 28). *Going Virtual with PrEP Service Delivery*. https://www.prepwatch.org/wp-content/uploads/2020/06/May28_2020_PrEPLearningNetwork_GoingVirtualServiceDelivery.pdf

[39] AVAC. (2020). *Policy and Health System Barriers and Enablers for the DPP*. On file with AVAC.

[40] AVAC & Matchboxology. (2021). *Dual Prevention Pill: A Summary of Insights and Recommendations on the uptake of the combined PrEP and Oral Contraceptive pill by women of reproductive age in SA and Zimbabwe*. https://www.prepwatch.org/wp-content/uploads/2021/08/2021_07_30-End-user-findings-summary_public.pdf

[41] AVAC & Matchboxology. (2020). *Dual Prevention Pill, South Africa and Zimbabwe: Digging for Insights*. On file with AVAC.

[42] *See* Smit, J. A., Church, K., Milford, C. et al. (2012). Key informant perspectives on policy- and service-level challenges and opportunities for delivering integrated sexual and reproductive health and HIV care in South Africa. *BMC Health Serv Res, 12*, 48. https://doi.org/10.1186/1472-6963-12-48

[43] See PMM. (2019). *HIV & Sexual and Reproductive Health Integration, Key Learnings from a Multipronged Review of Policies and Evidence.* https://www.avac.org/sites/default/files/resource-files/HIV_SRH_IntegrationDeck.pdf

[44] AVAC & Matchboxology. (2020). *Dual Prevention Pill, South Africa and Zimbabwe: Digging for Insights*. On file with AVAC; AVAC & Matchboxology. (2021). *Dual Prevention Pill, The Eureka Workshops and Solutions.* https://www.prepwatch.org/wp-content/uploads/2021/08/2021_07_30-DPP-Eureka-workshop-recommendations_public.pdf; CONRAD. *Project V, Research Summary.* https://www.conrad.org/launchingv/research/

[45] AVAC & Matchboxology. (2021). *Dual Prevention Pill, The Eureka Workshops and Solutions*. https://www.prepwatch.org/wp-content/uploads/2021/08/2021_07_30-DPP-Eureka-workshop-recommendations_public.pdf

[46] CHAI. *HIV New Product Introduction Toolkit*. https://www.newhivdrugs.org/procurement-planning; KKEMSA. *Tenders*. https://www.kemsa.co.ke/tenders/

[47] Mann Global Health. (2019). *Donor Funding Landscape for Condom Programming*. On file with AVAC.

[48] CHAI. (2021). Dual Prevention Pill Cost of Goods (COGS) Analysis. On file with AVAC. See also The Global Fund. (2020). *Pooled Procurement Mechanism Reference Pricing: ARVs*. https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf; CHAI. (2019). *Family Planning Market Report*. https://www.clintonhealthaccess.org/family-planning-market-report/; Guttmacher Institute. (2020). *Adding it Up: Investing in Sexual and Reproductive Health 2019*. https://www.guttmacher.org/report/adding-it-up-investing-in-sexual-reproductive-health-2019

[49] Funders Concerned about AIDS. (2020). *Philanthropic Support to Address HIV/AIDS in 2018*. https://www.fcaaids.org/wp-content/uploads/2020/03/ULTIMATE-2018-FCAA-RT-Report.pdf; amfAR. *PEPFAR Country/Regional Operating Plans (COPs/ROPs) Database*. https://copsdata.amfar.org/s/2020/(Subprog)%20PrEP

[50] UNAIDS. *AIDSInfo*. https://aidsinfo.unaids.org/

[51] UNFPA. *World Population Dashboard*. https://www.unfpa.org/data/world-population-dashboard

[52] *See* FP2020. *Core Indicator Summary Sheet: 2018-2019 Annual Progress Reports; Kenya, Malawi, South Africa, Uganda, Zambia, Zimbabwe country pages*. https://familyplanning2020.org/; United Nations Department of Economic and Social Affairs. (2020). *Contraceptive Use by Method 2019*. https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Jan/un_2019_contraceptiveusebymethod_databooklet.pdf (source for Botswana, Eswatini data)

[53] AVAC. *PrEPWatch.* https://www.prepwatch.org/

[54] AVAC. (2021). *Global PrEP Tracker.* https://data.prepwatch.org/

[55] FP2020. *Track20, Family Planning Effort Index (FPE)*. http://track20.org/pages/data_analysis/policy/FPE.php

[56] IPM. *Dapivirine ring*. https://www.ipmglobal.org/our-work/our-products/dapivirine-ring

[57] AVAC. (2021). *An Advocates' Primer on Long-Acting Injectable Cabotegravir for PrEP: Understanding the Initial Results of HPTN 083 & HPTN 084*. https://www.avac.org/primer-long-acting-injectable-prep

[58] Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. (2019). HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. *The Lancet*, 394(10195), 303-313. https://doi.org/10.1016/S0140-6736(19)31288-7

[59] PEPFAR. (2017). *Strategy for Accelerating HIV/AIDS Epidemic Control (2017-2020)*. https://www.state.gov/wp-content/uploads/2019/08/PEPFAR-Strategy-for-Accelerating-HIVAIDS-Epidemic-Control-2017-2020.pdf; PEPFAR. (2021). *2021 Annual Report to Congress*. https://www.state.gov/wp-content/uploads/2021/02/PEPFAR2021AnnualReporttoCongress.pdf

[60] The Global Fund. (2020). *Technical Brief: HIV Programming for Adolescent Girls and Young Women in High-HIV Burden Settings*. https://www.theglobalfund.org/media/4576/core_adolescentgirlsandyoungwomen_technicalbrief_en.pdf

[61] UNFPA. (2017). *UNFPA strategic plan, 2018-2021, Annex 4, Business mode*l. https://www.unfpa.org/sites/default/files/admin-resource/UNFPA_strategic_plan_2018-2021._Annex_4_-_Business_model_-_FINAL_-_24Jul17.pdf

Dual Prevention Pill

Market Preparation and Introduction Strategy

AVAC 25 Years and Counting

CLINTON HEALTH ACCESS INITIATIVE

HIV Prevention Market Manager
Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact
AVAC 25 Years and Counting
Supported by the Bill & Melinda Gates Foundation

Mann Global Health

CIFF CHILDREN'S INVESTMENT FUND FOUNDATION